UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/724,194	12/01/2003	John Fitzgerald Kokai-Kun	SYNI-007RCE3	1338

959 7590 08/06/2010

LAHIVE & COCKFIELD, LLP
FLOOR 30, SUITE 3000
ONE POST OFFICE SQUARE
BOSTON, MA 02109

EXAMINER	
PORTNER, VIRGINIA ALLEN	
ART UNIT	PAPER NUMBER
1645	
MAIL DATE	DELIVERY MODE
08/06/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/724,194	KOKAI-KUN ET AL.	
	Examiner	Art Unit	
	GINNY PORTNER	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18,21-25 and 39-58* is/are pending in the application.

4a) Of the above claim(s) *39-58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18 and 21-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *5/17/2010* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 18, 21-25, 39-58 are pending. Claim 28 has been canceled.
Claims 18 and 21-25 are under consideration.
Claims 39-58 remain withdrawn from consideration.

Objections/Rejections Withdrawn

1. Withdrawn, ***Drawings*** In addition to Replacement Sheets containing the corrected drawing figure(s), applicant is required to submit a marked-up copy of each Replacement Sheet including annotations indicating the changes made to the previous version. The marked-up copy must be clearly labeled as "Annotated Sheets" and must be presented in the amendment or remarks section that explains the change(s) to the drawings. See 37 CFR 1.121(d)(1). Failure to timely submit the proposed drawing and marked-up copy will result in the abandonment of the application. Figure 4 continued was submitted in Amended form, together with a Mark-up copy of the amended figure, thus obviating the objection.
2. Withdrawn, ***Claim Objections*** Claim 28 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 28 recites the composition of claim 18 together with a pharmaceutically acceptable carrier. In light of the amendment of claim 18 to now require the presence of a pharmaceutically acceptable carrier, the composition of claim 28 is no longer further limiting of the composition of claim 18. Claim 28 has been canceled.
3. Withdrawn, Claim 28 objected to because of the following informalities: Claim 28 recites the phrase: "A passive immunotherapy comprising"; a transitional phrase is missing, specifically the term ----composition--- following the term "immunotherapy". Claim 28 is a composition claim and should be clearly set forth as such. If claim 28 is not amended to clearly define the claim as a composition this objection will be maintained; if claim 28 is amended to a non-elected category of invention, the claim will be withdrawn from consideration as the claim has always been examined as a composition claim based upon the recited components following the term "comprising" which are composition components. Claim 28 has been canceled.
4. ***Withdrawn, Double Patenting*** The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d

887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. **Withdrawn**, Claims 18, 21-25 and 28 rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 and 7-10 of U.S. Patent No. 7,169,903 is herein withdrawn in light of the claims having been amended to require the claimed antibody to bind to ribitol phosphate, and US Pat. 7,169,903 teaches the generic binding to any carbohydrate, and does not specifically claim nor mention antibodies with binding specificity to ribitol phosphate present in LTA of S. aureus. Applicant's amendment of the claims has obviated the obviousness type double patenting rejection.

6. Withdrawn, Claim 18 and 28 rejected under 35 U.S.C. 102(b) as being anticipated by Aasjord et al (1985) in light of independent claim 18 being amended to be limited to ribitol phosphate, and the monoclonal antibodies of Aasjord et al are specific to Satphylococcus aureus β-N-acetylglucosaminyl of ribitol teichoic acid

Objections/Rejections Maintained/ Response to Arguments

7. Applicant's arguments filed May 17, 2010 have been fully considered but they are not persuasive.

Specification

8. The amendment of Specification paragraph [0031] filed May 17, 2010 in response to the New Matter rejection made of record in the Office Action dated January 15, 2010 which pointed out that the Applicant's amendment submitted June 30, 2009 added material which is not supported by the original disclosure nor Figure 1, sought to resolve the issue of the phrase "such

as" by submitting the following amendment :

Please amend the specification as follows:

[031] Figure 1 shows the structure of *S. aureus* WTA and disruption of WTA production. *A.* Structure of *S. aureus* WTA. The N-acetylglucosamine (GlcNAc) phosphate and D-alanine portions are depicted in braces. MurNAc, *N*-acetylmuramic acid. Components of the structure are further labeled with the genes or operons, ~~such as TagO and DltABCD,~~ which are involved in the structure's synthesis including, TagO and DltABCD.

9. The phrase "including, TagO and DltABCD" suggests more than what is shown in Figure 1. Therefore the brief description of the figures for Figure 1 still contains New Matter because *Figure 1 does not show multiple types of genes or operons* involved in the structure's synthesis, but only shows TagO and DltABCD. The Brief Description of Drawing Figure 1 should refer to only TagO and DltABCD. --------Components of Figure 1A labeled with TagO and DltABCD represent the coding sequence and operon for the synthesis of N-acetylglucosamine (GlcNAc) phosphate and D-alanine structures, respectively, within the Staphylococcus aureus ribitol teichoic acid shown. -------- or an equivalent phrase that evidences original descriptive support. Additionally the amendment of paragraph [0031] should include the submission of entire paragraph [0031] which also describes frames B, C and D of Figure 1, not just Frame A. Below is the original description of Figure 1 which should be modified to include the narrative required for a complete description of Figure 1, Frame A .

[031] Figure 1 shows the structure of *S. aureus* WTA and disruption of WTA production. **A.** Structure of *S. aureus* WTA. The *N*-acetylglucosamine (GlcNAc) phosphate and D-alanine portions are highlighted with gray boxes. MurNAc, *N*-acetylmuramic acid. **B.** Location of the *S. aureus tagO* gene and strategy for its replacement with the *ermB* cassette. **C.** Polyacrylamide gel with WTA preparations stained with a combined alcian blue and silver stain procedure. **D.** The *ΔtagO* mutant is deficient in WTA. Analysis of the content of phosphate, GlcNAc, and ribitol in WTA preparations from *S. aureus* Sa113 wild-type (WT), *ΔtagO* mutant (M) and *ΔtagO* complemented with plasmid pRBtagO (MC). The mean and SD of at least five independent experiments (phosphate, GlcNAc) or the mean of four counts from one experiment (ribitol) are shown. Ribitol content was determined in WT and M samples only.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. **Maintained**, The rejection of claims 18, and 21-25 under 35 U.S.C. 103(a) as being unpatentable over Gotz and Peschel (common inventor, DE19912706) et al in light of English translation, in view of Fischer (reference of record, US Pat. 6,939,543, filing date June 2001) in view of Patti (US Pat. 6,703,025, filing date August 31, 1999) is traversed on the grounds that:

a. The examiner has overstated the teachings of Gotz et al;

b. That Gotz et al. teaches away from the instant invention because the reference is directed to a method of treatment of bacterial infection with teichoic acid synthesis inhibitors;

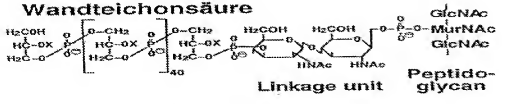
c. Gotz et al. does not teach anti-ribitol teichoic acid antibodies induced to the WTA of Staphylococcus aureus strain Sa113;

d. Gotz et al do not disclose any correlation between the antiserum described in the cited paragraph and the ribitol phosphate WTA depicted in Figure 1.

12. Gotz et al do teach the chemical structure of ribitol wall teichoic acid for Staphylococcus aureus strain Sa113 (see De 19912706, figure 1, Wandteichonsaure) and polyclonal antibodies directed thereto which recognize alanine substituted or non-substituted ribitol wall teichoic acid (see English machine translation page 4, p. 2, line 7),

fluorescences, or with antiserums, which recognize specific alanine-substituted or non-substituted Teichonsauren.

the ribitol teichoic acid being from a gram positive bacteria, the structure of which is exemplified in Figure 1, Staphylococcus aureus strain Sa113; a non-substituted ribitol teichoic acid would produce/induce antibodies/antisera to ribitol phosphate of the structure shown in Figure 1 without the alanine substitution :



13.

Gotz et al do teach the treatment of teichoic acid synthesis inhibitors, as well as active

agent treatment for removal of D-alanine ribitol teichoic acid to make S. aureus more susceptible to *antimicrobial substances*

> substances. These meant that by an inhibition of the alanine installation the bacteria become more sensitive opposite antimicrobial substances, and are in this way open to attack. This result opens a complete new aspect for a Wirkstoffindung, as the alanine installation in Teichonsäuren becomes a chosen as point of attack for the active ingredients which can be developed.

Gotz et al teach that after treatment and removal of D-alanine, an antimicrobial substance can be used more effectively to eliminate the Gram positive bacteria (English translation, page 2, paragraph 4), including staphylococci (Eng. Trans. Page 2, p. 2, line 3),

> After the treatment with the active ingredients according to invention the Gram positive bactena can be eliminated by the antimicrobial substances. Without this corresponding treatment the bacteria are resistant opposite these substances. The antimicrobial substances can be without an application in the body present,

specifically Staphylococcus aureus (Eng. Trans. Page 1, p. 2, line 8), as well as block binding to cell receptors (claim 22 (increased affects by antimicrobial substances), claim 19 (decreased/reduced inflammatory effects on cells), claim 25 (reduced biofilm formation in vivo (prevent sepsis, or on inert surfaces (also see Eng. Trans. Pg. 2, p. 5).

Gotz et al differed from the instantly claimed invention by failing to show the anti-ribitol wall teichoic acid antibodies to be monoclonal antibodies and the antimicrobial substance to be antibodies which could be used to more effectively eliminate Staphylococcus aureus pathogens from nasal infection.

14. Fischer et al teach how the make and use polyclonal, monoclonal, chimeric, human and humanized antibodies for anti-teichoic antibodies (see col. 22, lines 48-52, col. 5, lines 32-40), teach Staphylococcus aureus produces ribitol teichoic acid (see col. 5, lines 32-35;see col. 22, lines 30-35 and 48-52), abstract and col. 2, line 2), wherein anti-teichoic acid antibodies provide for increased opsonization and phagocytosis of S. aureus (see col. 22, lines 30-35 and 48-52) and

the antibodies can therefore serve as an antimicrobial substance for the effective elimination of Staphylococcus aureus.

15. Patti et al teach pharmaceutical compositions (see col. 8, lines 20-23; col. 39, line 34) that comprise antibodies (see col. 39, lines 32-35), the antibodies including anti-teichoic acid antibodies (see col. 39, line 35 "as described above) specific for ribitol teichoic acid (see col. 22, lines 48-52 and lines 36-47 "opsonic antibodies") together with a pharmaceutically acceptable carrier (see col. 39, lines 36-37) in a therapeutically effective amount (see col. 40, lines 14-15) administrable by an intranasal route (nasogastric (col. 28, line 66) or nasopharyngeal (col. 44, line 15) for the purpose of passive immunization (see col. 9, lines 1-2) and blocking colonization of S. aureus in the nose of a subject (col. 5, line 39).

Gotz et al in combination with Fischer and Patti obviate the instantly claimed invention because Patti et al teach anti-ribitol teichoic acid antibodies provide for increased opsonization and phagocytosis/elimination of Staphylococcus aureus and thus function as an antimicrobial substance specific to ribitol wall teichoic acid containing pathogens and Fischer et al teach ribitol teichoic acids are major antigens in the cell of gram positive/Staphylococcal pathogens to include Staphylococcus aureus and teach the production of monoclonal antibodies are highly specific to the antigen to which they bind and are not dependent on animals for production.

The person of ordinary skill in the art would have been motivated by the reasonable expectation of success of obtaining monoclonal anti-ribitol teichoic acid antibody compositions directed to the S. aureus cell wall antigen of Gotz et al, because Patti et al teaches that through using ribitol phosphate linked to peptidoglycan, the teichoic acids are antigenic and anti-teichoic acid antibodies are produced (see col. 22, lines 48-52) and Fischer et al teach and provide

motivation for the production of monoclonal antibodies, and recombinant antibodies and fragments that specifically bind to ribitol teichoic acid, the anti-ribitol teichoic acid antibodies serving as antimicrobial substances that provide for the generation of vaccines and other therapeutics (see Fischer abstract). In re Erlich 1988 teaches that it is obvious to make a monoclonal antibody to an antigen to which a polyclonal antibody is known.

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method , and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar element according to known methods is likely to be obvious when it does no more than yield predictable results". It well known in the art to use monoclonal antibodies for formulation of compositions to a specific ribitol teichoic acid, the guidance and teaching of the references provide a solution to providing a ready source of specific antibodies that maintain their specific binding characteristics, and reduces the dependence upon immunization of animals to produce an antibody containing antisera that would vary upon the immune systems of different animals. Thus, it would be obvious to apply a known technique (monoclonal antibody production) to a known product (generation of antibody containing antiserum specific to ribitol wall teichoic acid) to be used in a known method (generation and formulation of monoclonal antibody compositions) that is ready for improvement of having a ready sources of ribitol specific antibodies for the formulation of pharmaceutical compositions. Gotz et al in view Fischer and Patti obviated the instantly claimed invention as now claimed.

New Claim amendment/Reinstated or New Grounds of Rejection/Objection

Claim Objections

16. Claims 21-24 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 18 from which claims 21-24 depend has been amended to be directed to a composition of monoclonal antibodies specific to ribitol in wall teichoic acid. Dependent claims 21-24 are specific to WTA (wall teichoic acid) and therefore are not limited to ribitol specific antibodies. Claims 21-24 are not further limiting of amended claim 18 as claims 21-24 have a broader scope than independent claim 18 from which they depend. Claims 21-24 should recite --- further comprises ------ to obviate this objection.

Claim Rejections - 35 USC § 102.

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

18. Claims 18 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Hunter et al (US Pat. 4,954,449, reference of record)in light of extrinsic evidence provided by Argaman et al (1974, reference of record).

19. Hunter et al disclose compositions of human monoclonal antibodies directed to polyribosyl ribitol phosphate together with a pharmaceutically acceptable carrier (see col. 3, lines 14-19 and lines 29-32), the antibodies being present in the composition in a therapeutically effective amount (see claim 2) and can provide passive prophylaxis (see Hunter et al, col. 6, line 22).

20. The monoclonal antibodies in the composition are directed to pathogenic bacteria that comprise poly ribitol phosphate, and in light of evidence provided by Argaman et al who show antibody cross reactivity between H. influenza and Staphylococcus aureus (see Argamon et al, abstract and figure 2, page 652) ribitol phosphate teichoic acid exists, inherently the compositions of Hunter et al anticipate the instantly claimed invention as now claimed.

21. Inherently the reference anticipates the now claimed invention. Atlas Powder Co. V IRECA, 51 USPQ2d 1943, (FED Cir. 1999) states Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art...However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior arts functioning, does not render the old composition patentably new to the discoverer. The Court further held that this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art.

Claim Rejections - 35 USC § 103

22. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

23. Claims 18, and 21-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer et al (US Pat. 6,939,543, filing date June 2001, reference of record) in view of Patti (US Pat. 6,703,025, filing date August 31, 1999, reference of record) .

24. Fischer et al teach monoclonal antibodies that bind specifically to ribitol phosphate teichoic acid of S. aureus. Fischer et al specifically teach the teichoic acids of Staphylococcus aureus to comprise ribitol phosphate or glycerol phosphate teichoic acid (see col. 5, lines 32-35), and Fischer et al states their antibodies are directed to "LTA exposed on the surface of the cell wall of Gram positive bacteria (paragraph 2)" and goes on to state: "Teichoic acids are polymers of either glycerol phosphate or ribitol phosphate with various sugars (paragraph 3) " .

25. Fischer teaches and suggests combination compositions of antibodies directed to ribitol phosphate and glycerol phosphate antigens. It has long been held that a reference must be evaluated in its entirety, not on the basis of its preferred embodiments or working examples. *In re Mills*, 470 F.2d 649, 651, 176 (USPQ 198 (CCPA 1972).While a focus of Fischer et al is directed to the production of anti-glycerol teichoic acid antibodies, the reference also describes the production of additional antibodies to Staphylococcus aureus lipoteichoic acid to include ribitol teichoic acid.

26. Fischer et al teach "The present invention encompasses monoclonal and chimeric antibodies that bind to lipoteichoic acid of Gram positive bacteria. The antibodies also bind to whole bacteria and enhance phagocytosis and killing of the bacteria in vitro and enhance protection from lethal infection in vivo. The mouse monoclonal antibody has been humanized and the resulting chimeric antibody provides a previously unknown means to diagnose, prevent

and/or treat infections caused by gram positive bacteria bearing lipoteichoic acid. This invention also encompasses a peptide mimic of the lipoteichoic acid epitope binding site defined by the monoclonal antibody. This epitope or epitope peptide mimic identifies other antibodies that may bind to the lipoteichoic acid epitope. Moreover, the epitope or epitope peptide mimic provides a valuable substrate for the generation of vaccines or other therapeutics." That antibodies are specific for Gram positive bacterial lipoteichoic acid.

27.

Fischer et al describe their "FIELD OF THE INVENTION" to include:

"This invention in the fields of immunology and infectious diseases relates to antibodies that are specific for Gram positive bacteria, particularly to lipoteichoic acids exposed on the surface of the bacteria" for the purpose of [0010], treating Staphylococcal infection:

> e. Staphylococcal infections are difficult to treat for a variety of reasons. Resistance to antibiotics is common and becoming more so. See L. Garrett, The Coming Plague, "The Revenge of the Germs or Just Keep Inventing New Drugs" Ch. 13, pgs. 411-456, Farrar, Straus and Giroux, NY, Eds. (1994). In one study, the majority of Staphylococci isolated from blood cultures of septic infants were multiply resistant to antibiotics (A. Fleer et al., Pediatr. Infect. Dis. 2:426 (1983)). A more recent study describes methicillin-resistant S. aureus (J. Romero-Vivas, et al., Clin. Infect. Dis. 21:1417-23 (1995)) and a recent review notes that the emergence of antibiotic resistance among clinical isolates makes treatment difficult (J. Lee., Trends in Micro. 4(4):162-66 (April 1996). Recent reports in the popular press also describe troubling incidents of antibiotic resistance. See The Washington Post "Microbe in Hospital Infections Show Resistance to Antibiotics," May 29,1997; The Washington Times, "Deadly bacteria outwits antibiotics," May 29, 1997.

Fischer et al describe Staphylococcal infection to include both coagulase positive (S. aureus) and negative (S. epidermidis) types of Staphylococcus:

> Accordingly, there is a need in the art to provide monoclonal antibodies that can bind to Staphylococcus of both coagulase types and that can enhance phagocytosis and killing of the bacteria and thereby enhance protection in vivo. There is also a need in the

art for the epitope of the site to which such antibodies can bind so that other antibodies with similar abilities can be identified and isolated.

Fischer et al teach their compositions of antibodies to be opsonic and protective monoclonal and chimeric antibodies … of Gram positive bacteria.

> "To address these needs in the art, the present invention encompasses opsonic and protective monoclonal and chimeric antibodies that bind to lipoteichoic acid of Gram positive bacteria. The antibodies also bind to whole bacteria and enhance phagocytosis and killing of the bacteria in vitro and enhance protection from lethal infection in vivo. The mouse monoclonal antibody has been humanized and the resulting chimeric antibody provides a previously unknown means to diagnose, prevent and/or treat infections caused by gram positive bacteria bearing lipoteichoic acids. This invention also encompasses a peptide mimic of the lipoteichoic acid epitope binding site defined by the monoclonal antibody. This epitope or epitope peptide mimic identifies other antibodies that may bind to the lipoteichoic acid epitope. Moreover, the epitope or epitope peptide mimic provides a valuable substrate for the generation of vaccines or other therapeutics."

28. Fischer et al describes compositions of antibodies for antibody therapy (see col. 11, lines 16-18 and col. 11, lines 32-34), the compositions comprising antibodies specific for both types of teichoic acid antigens, to include ribitol teichoic acid specific monoclonal antibodies (see col. 11, lines 41-50).

29. The Fischer et al teach the importance of producing protective antibodies directed to gram positive bacteria, to include Staphylococcus aureus and epidermidis. Fischer et al goes on to teach the production of polyclonal, monoclonal, chimeric, human and humanized antibodies to S. aureus teichoic acids and suggests antibodies to glycerol and ribitol phosphate antigens.

30. Fischer et al teach the formulation of anti-LTA ribitol antibodies into pharmaceutical compositions that comprise a "therapeutically effective amount of a pharmaceutical composition comprising the anti-LTA immunoglobulin (whether polyclonal or monoclonal or chimeric, including fragments, regions and derivative thereof) and a pharmaceutically acceptable carrier."

31. Fischer et al differs from the instantly claimed invention by failing to show compositions that comprise a therapeutically effective amount of antibodies to include ribitol phosphate antibodies of cell wall teichoic acid.

32. Patti et al teach the production of antibodies to ribitol phosphate (Detailed Description Text (95)) present in cell wall Teichoic acids, and lipoteichoic acid, wherein the ribitol phosphate is a polymer linked to the peptidolglycan and is a known antigen in an analogous art for the purposes of producing anti-teichoic antibodies (see col. 22, lines 48-52) associated with staphylococcal antigens (abstract) that will serve to increase the opsonization and phagocytosis of S. aureus (see col. 22, lines 30-35 and 48-52). Patti et al show ribitol phosphate is immunogenic, and induces antibodies, wherein polyclonal antibodies to ribitol phosphate have been made. Patti et al teach and suggest "Multicomponent vaccines" and utlize teichoic acid epitopes to stimulate antibodies that induce cross reactive antibodies, as well as teach glycerol and ribitol phosphate induce anti-teichoic antibodies:

> US 6703025 B1 Detailed Description Text (25):
> As used herein, an "antigenically functional equivalent" protein or peptide is one that incorporates an epitope that is immunologically cross-reactive with one or more epitopes either derived from any of the particular MSCRAMM proteins disclosed ….derived from any of the particular bacterial components disclosed (e.g., teichoic acids, alpha toxin and capsular polysaccharide type 5). Antigenically functional equivalents, or epitopic sequences, may be first designed or predicted and then tested, or may simply be directly tested for cross-reactivity.

33. Fischer et al in view of Patti et al provide guidance, teaching, suggestion and motivation to make monoclonal, chimeric, humanized and human antibodies to ribitol teichoic acid, a wall component of known human pathogenic strains of Staphylococcus aureus because Fischer et al teach antibodies directed to lipoteichoic acids(LTA) "can block the binding of Gram positive

bacteria to epithelial cells, such as human epithelial cells (Fischer et al, first paragraph)" and Patti et al teach ribitol phosphate is immunogenic and induces antibodies directed to S.aureus wall teichoic acid as well as LTA , wherein anti-ribitol phosphate wall teichoic acid antibodies can serve to enhance opsonization and phagocytosis of S.aureus. It is obvious to make a monoclonal antibody to an antigen for which polyclonal antibodies has been made. In re Erlich, 1988. Fischer et al in view of Patti et al obviate the instantly claimed invention as now claimed.

Conclusion

34. This is a Final action.

35. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

36. Any inquiry concerning this communication or earlier communications from the examiner should be directed to GINNY PORTNER whose telephone number is (571)272-0862. The examiner can normally be reached on flextime, but usually M-F, alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Robert B Mondesi/
Supervisory Patent Examiner,
Art Unit 1645

/Ginny Portner/
Examiner, Art Unit 1645
August 3, 2010